WO 2005/093097

1/17

PCT/FR2005/000656

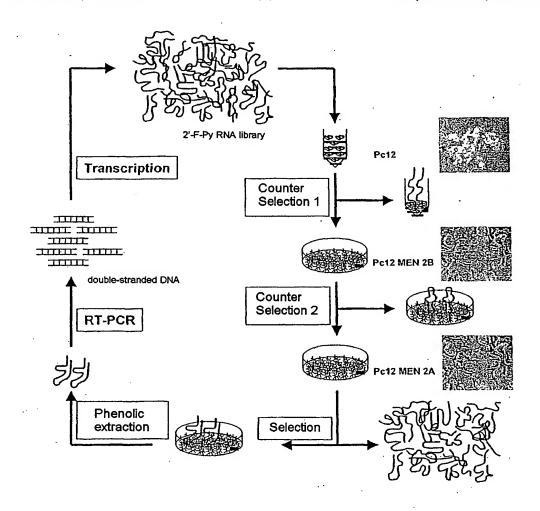
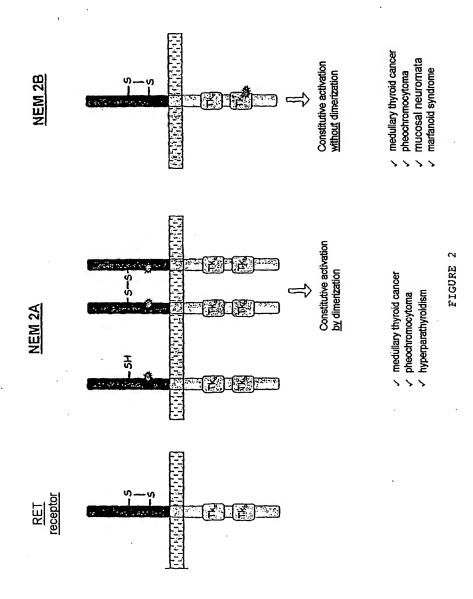
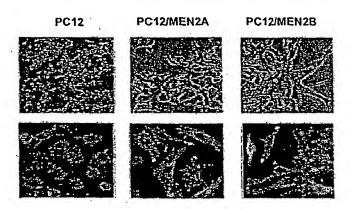


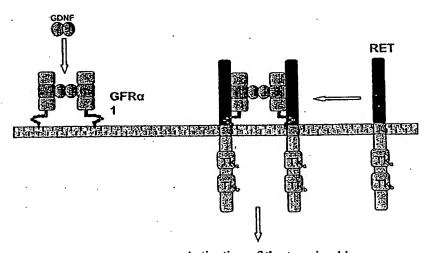
FIGURE 1



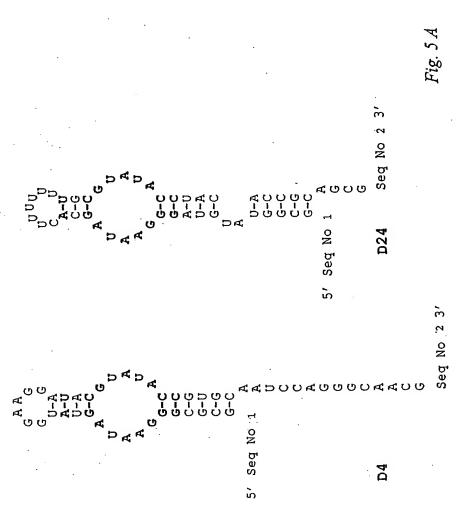


PC12 cells stably transfected with a vector for expression of the human mutated receptors Ret^{C634Y} (PC12/ MEN2A) or Ret^{M918T} (PC12/MEN2B).

Diagrammatic representation of GDNF-dependent RET receptor activation



Activation of the tyrosine kinase



73

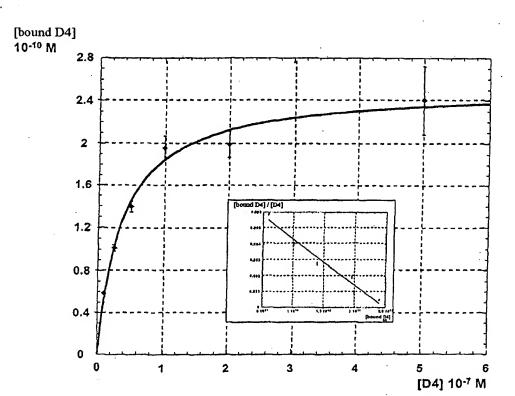
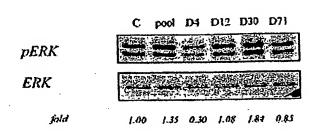


FIGURE 5B

•

-

A



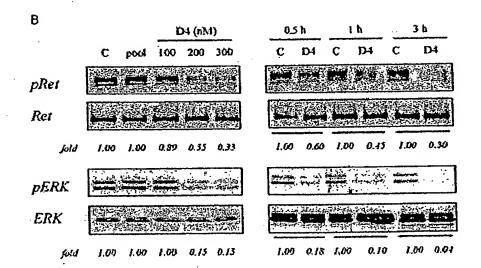
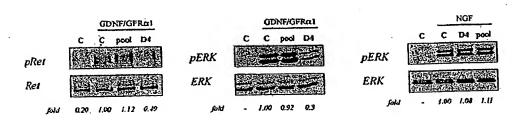


FIGURE 6



PRet PERK

Ret ERK

Gill 1.00 1.00 9.99 PM

FIGURE 7 .

PC12-\alpha1/wt cells

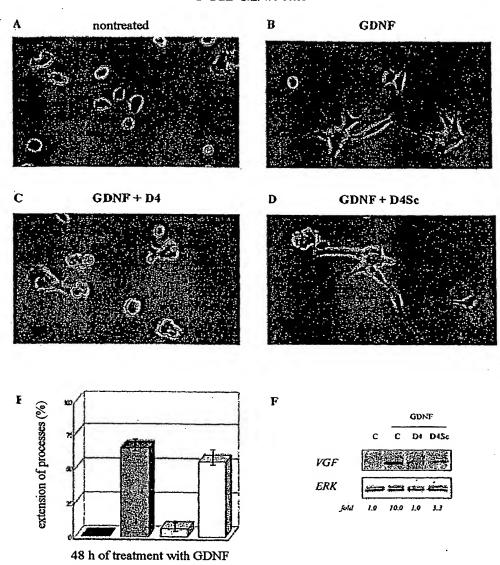


FIGURE 8

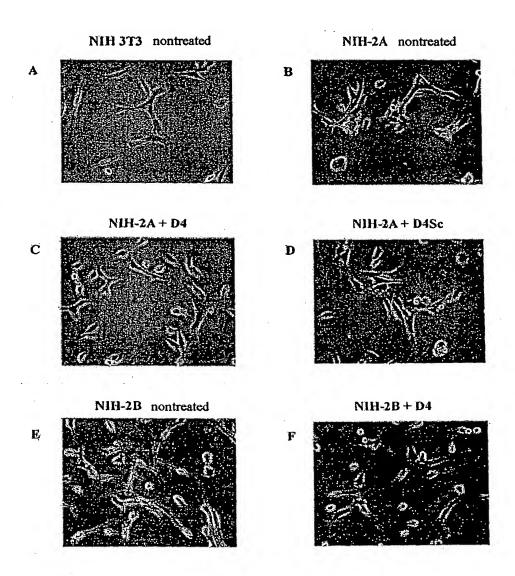
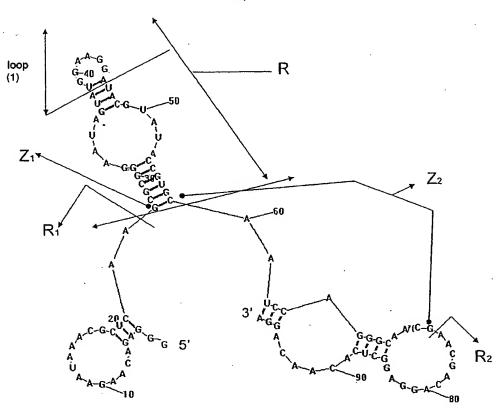


FIGURE 9

$$X_1 - X_1$$
 $X_2 - X_2'$
 $X_3 - X_2'$
 $X_4 - X_4'$
 $X_3 - X_3'$
 $X_4 - X_4'$
 $X_5 - X_5$
 $X_6 - X_6'$
 $X_4 - X_6'$
 $X_5 - X_5$
 $X_6 - X_6'$
 $X_6 -$



D4 - 97nt ENERGY -17.5

FIGURE 11

5' → 3'

 $R_1 + Z_1 = R_4$

5' → 3'

 $R_2 + Z_2 = R_5$

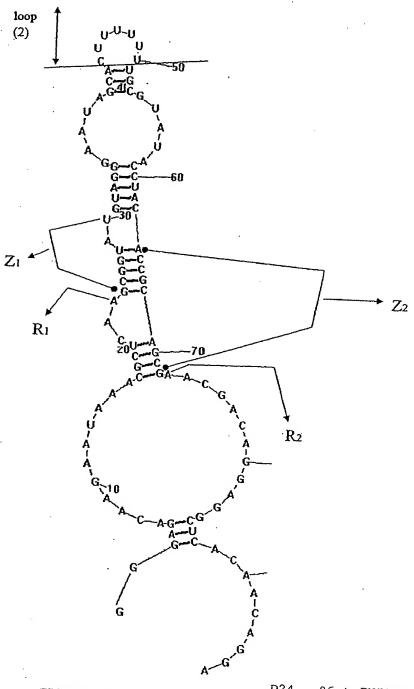
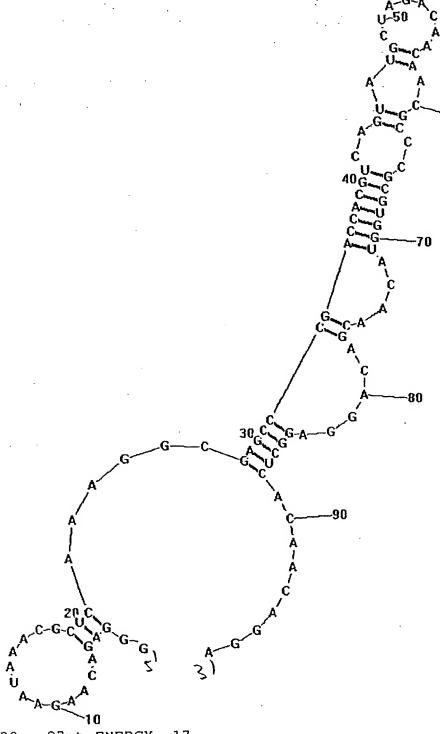


FIGURE 12

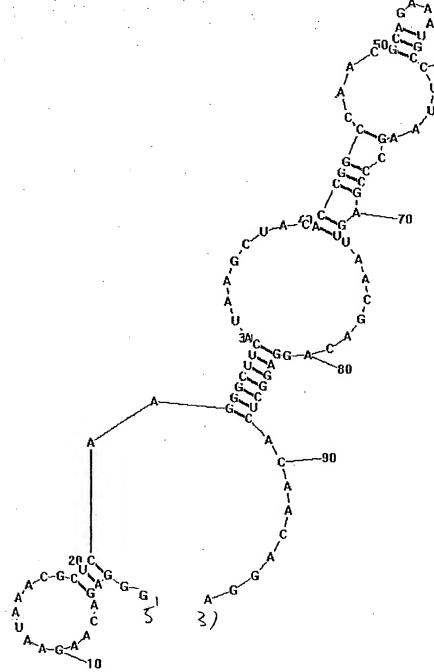
D24 - 96nt ENERGY -24

$$R_1 + Z_1 = R_4$$

$$R_2 + Z_2 = R_5$$

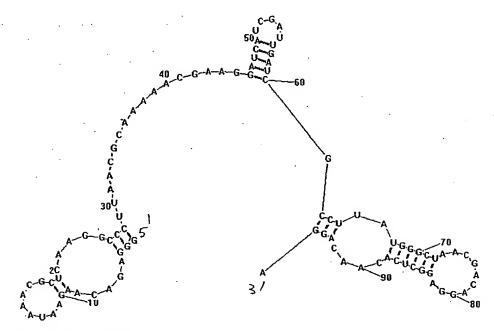


D30 - 97nt ENERGY -17



D12 - 97nt ENERGY -19.1

FIGURE 14



D71 - 96nt ENERGY -16.6

Fig. 16: Screening of aptamers which interact with RET on PC12 MEN 2A cells by competitive binding with the D4 aptamer

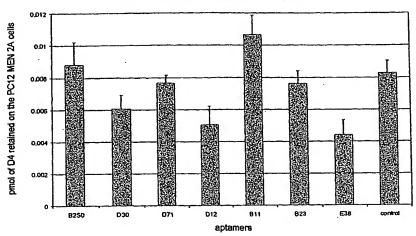


Fig. 17: Competitive binding of the E38 aptamer on PC12 MEN 2A cells in the presence of an increasing concentration of D4 aptamer

